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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/549,648	09/15/2005	Gregor Sagner	21810-US	2235

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ROCHE MOLECULAR SYSTEMS INC
PATENT LAW DEPARTMENT
1145 ATLANTIC AVENUE
ALAMEDA, CA 94501

EXAMINER	
PANDE, SUCHIRA	

ART UNIT	PAPER NUMBER
1637	

MAIL DATE	DELIVERY MODE
06/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/549,648	SAGNER ET AL.	
	Examiner	Art Unit	
	Suchira Pande	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-17* is/are pending in the application.

4a) Of the above claim(s) *1-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *15-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/5/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

1. Applicant's election without traverse of group IV invention claims 15-17, in the reply filed on May 4, 2007 is acknowledged.

2. Claims 1-14 withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 4, 2007. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claim 15 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15, recites ----" by at least 25 and preferably at least 30 nm"-----"at least 3, preferably 4 and most preferably 5 differently labeled FRET" -----. The

recitation of preferred embodiment within the claimed range renders the claim indefinite.

Use of a narrow numerical range that falls within a broader range in the same claim may render the claim indefinite when the boundaries of the claim are not discernible. If stated in a single claim, examples and preferences lead to confusion over the intended scope of the claim.

While a single claim that includes both a broad and a narrower range may be indefinite, it is not improper under 35 U.S.C. **112**, second paragraph, to present a dependent claim that sets forth a narrower range for an element than the range set forth in the claim from which it depends. Thus claims 16 and 17 are proper dependent claims. See MPEP 2173.05 (c).

Claim Interpretation

5. Claim 15 is indefinite as pointed out above. In the interest of compact prosecution for applying art, claim 15 is being read to comprise "at least 1 light source, 5 fluorescent detector entities,---the detection wavelength of each entity distinct from each other by at least 25 nm,-----simultaneously detecting maximum fluorescence of at least 3 differently labeled FRET hybridization probe pairs---".

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 15-17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bell and Ranford-Cartwright (2002) Trends in Parasitology Vol. 18, No.8. pp-337-342 (provided by applicant in IDS) as evidenced by Wittwer et al. (1997) Biotechniques vol. 22, No.1 pp176-181, in view of Hiratsuka et al. (2002) Clinical Biochemistry vol. 35 (1) Pages 35-40; Epstein et al. (2002) Analytica Chimica Acta 469: pp 3-36; Glazer et al. (US pat. 6,150,107 issued Nov 21, 2000)

Regarding claim 15, Ranford-Cartwright teach: real time PCR instrument (see page 339 Table 1 where comparison of 7 different real time PCR thermal cyclers is done. On page 339, Ranford-Cartwright teach LightCycler™ but do not recite structural details associated with this cycler. Wittwer et al. explicitly provides the structural details associated with LightCycler™ PCR instrument) comprising;

Wittwer et al. teach at least 1 light source, preferably an LED (See page 17 abstract where blue light-emitting diode (LED is taught).

Wittwer et al. teaches use of different filters for detection of SYBR® Green I (520-580 nm) , fluorescein (520-550 nm), rhodamine (580-620 nm) and Cy5™ (660-680 nm) dyes (see page 177 par. 3 and page 178 par. 1). Therefore they teach 3 fluorescent detector entities for the three colors fluorescein, rhodamine and Cy5™ , each of said entities having central detection wavelengths which are distinct from each other by at least 25 nm (As can be seen from the wavelengths taught above that central detection wavelengths are distinct from each other by at least 25 nm),

characterized in that said detector entities are capable of simultaneously detecting (see Ranford-Cartwright page 338 par. 3 where instruments capable of "simultaneous" scanning of samples thus decreasing total assay times are taught. By this teaching Ranford-Cartwright is teaching instrument capable of "simultaneously detecting") maximum fluorescene emission of differently labeled FRET Hybridization Probe pairs (see Ranford-Cartwright page 338 par. labeled "Dual hybridization probes" where detection of FRET Hybridization Probe pairs is taught),

simultaneously detecting maximum fluorescence emission of at least 2 differently labeled TaqMan hybridization probes (see Ranford-Cartwright page 338 par. labelled "Hydrolysis probes" where TAMRA and ROX labeled TaqMan hybridization probes are taught. Therefore Ranford-Cartwright teach instrument capable of simultaneously detecting maximum fluorescence emission of at least 2 differently labeled TaqMan hybridization probes) , and

detecting maximum fluorescence emission of SYBR® Green I (see Ranford-Cartwright page 338, par. labeled "Detection systems for quantification" where SYBR®

Green I detection is taught. Therefore Ranford-Cartwright teach instrument capable of detecting maximum fluorescence emission of SYBR® Green I.

Examiner would like to point out that all of the capabilities "detecting----FRET hyb probe pairs, ----TaqMan hyb-----, detecting fluorescence of SybrGreen I" recited above for the detector entity are only intended use and do not impart any structural limitation to the detector claimed. If the detector is capable of detecting the fluorescence then as far as the instrument is concerned it does not matter how the fluorescence was generated in the sample to be detected.

means for heating and cooling (See page 178 section labeled Commercial Light Cycler par. 2 where Wittwer et al. teaches heating cartridge and a motor that drives chamber fan as a means for heating. The heater is disabled and the fan is run at high speed as cooling means).

multiple reaction vessels for containing a reaction mixture (See Fig. 2 where Wittwer et al. teaches 24 sample carousel as multiple reaction vessels for containing a reaction mixture)

Regarding claim 16, Wittwer et al teaches a PCR instrument comprising exactly one light source (see claim 15 above where Blue light LED source is taught).

Claim 17, recites an instrument according to claim 15-16, characterized in that said central detection wavelengths are selected from a group of range of wavelengths, said group consisting of 520-540 nm, 545-565 nm, 570-590 nm, 600-620 nm, 630-650 nm, 660-680 nm, and 700-720 nm. The range of wavelengths recited only indicate

intended use and do not provide further structural limitation to the claimed instrument and hence are not being considered further.

Regarding claim 15, Wittwer et al. only teach 3 fluorescent detector entities. Also Wittwer et al. only teaches sequential detection.

Regarding claim 15, Ranford-Cartwright does teach simultaneous detection but does not explicitly teach 5 fluorescent detector entities.

Regarding claim 15, Hiratsuka et al. teach use of real time PCR for simultaneous fluorescent detection of 5 SNPs, on a single thermocylce protocol by the Light Cycler (see page 35 conclusion section) using FRET based hybridization probes (see page 36 par. 2). The above conclusion inherently indicates that the LightCycler instrument used by Hiratsuka et al. has 5 fluorescent detection entities.

It would have been prima facie obvious to one of ordinary skill in the art to practice the thermocycler having 5 fluorescent detector entities as taught by Hiratsuka et al. in the thermocyclers taught by Ranford-Cartwright as evidenced by Wittwer et al. at the time the invention was made.

The motivation to do so is provided to one of ordinary skill in the art by teachings of Epstein et al.

Epstein et al. while reviewing fluorescence –based nucleic acid detection and microarrays state "The Taqman assay is a solution based FRET method designed to perform quantitative PCR product measurements in real time. By monitoring the reaction progress with FRET techniques, the need for gel electrophoresis or repetitive sample handling can be avoided"-----(see Epstein et al. page 7 section 2.3.3 Taqman

real time PCR detection). They go on to state "Fluorescence measurements are made directly during the ongoing PCR cycles rather than at reaction completion. Taqman allows the reaction progress to be monitored in real time and is sensitive to single nucleotide polymorphisms" (see Epstein et al. page 9, par. 1).

In section 4.3.3. Epstein et al. describe the problems associated with FRET assays used for Pathogenic Microorganism (PM) detection namely the initial DNA target concentration can not be related to the amplified product fluorescence signal. In this context they state " To overcome this problem, FRET PCR strategies, including Taqman, have been developed using spectroflurometric-based thermal cyclers. These PCR assays offer a convenient and rapid assay to determine the total cell number in a sample.---------Different bacteria were detected using the real time PCR assays and the ABI Prism 7700 sequence detection system. The bacteria detected included *Listeria monocytogenes* (6-60 cells) in water and milk in <3h, one colony forming unit (CFU) of *Campylobacter jejuni* in < 3h and the total number of *Porphyromonas gingivalis* in dental plaque samples from periodontitis patients" (see Epstein et al. page 32 par. 1).

By having the capability to simultaneously detect many SNPs using different combinations of FRET and TaqMan probes in real time PCR would be valuable. So it behooves one of ordinary skill who knows the types of labels that are available and most suitable for use in FRET and TaqMan probe assays to develop a PCR machine that has detector capable of detecting all the pertinent wavelength ranges.

Glazer et al. provides information to one of ordinary skill regarding the various labels that can be used for FRET and the emission wavelengths that are used for their

detection. Thus providing guidance regarding what wavelength filters to use so that multiple fluorescent detectors will simultaneously detect fluorescence from appropriate regions. (See whole patent specially see col. 15 lines 24-42 and Fig. 4).

Conclusion

9. All claims under consideration 15-17 are rejected.

10. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suchira Pande whose telephone number is 571-272-9052. The examiner can normally be reached on 8:30 am -5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 571-272-0782. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Suchira Pande
Examiner

JEFFREY FREDMAN
PRIMARY EXAMINER

6/16/07

Art Unit 1637